

CLAIMS

1. A method of suppressing the expression of a selected gene in a eukaryotic cell the method comprising introducing into the cell (a) a
5 polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with the selected gene which site is present in a eukaryotic genome and a chromatin inactivation portion, or (b) a polynucleotide encoding said polypeptide.
- 10 2. A method according to Claim 1 wherein the nucleic acid binding portion is a DNA binding portion.
3. A method according to Claim 1 wherein the nucleic acid binding portion is an RNA binding portion and the site present in a eukaryotic
15 genome is a nascent RNA being transcribed from DNA.
4. A method according to any one of Claims 1 to 3 wherein the chromatin inactivation portion facilitates histone deacetylation.
- 20 5. A method according to any one of Claims 1 to 4 wherein the chromatin inactivation portion is all or a portion of a component of a histone deacetylation (HDAC) complex or all or a portion of a polypeptide which binds to or facilitates the recruitment of a HDAC complex.
- 25 6. A method according to Claim 5 wherein the component of the HDAC complex or the polypeptide which binds to or facilitates the recruitment of a HDAC complex is any one of PLZF, N-CoR, SMRT, Sin3, SAP18, SAP30 and HDAC.

7. A method according to Claim 6 wherein the chromatin inactivation portion is all or a N-CoR- or SMRT-binding part of PLZF.
- 5 8. A method according to Claim 6 wherein the chromatin inactivation portion is all or an enzymatically active part of a HDAC.
9. A method according to any one of Claims 2 to 6 wherein the DNA binding portion is all or a DNA-binding part of a zinc-finger DNA binding
10 protein or all or a DNA-binding part of a helix-turn-helix DNA binding protein.
10. A method according to Claim 9 wherein the DNA binding portion is all or a DNA-binding part of an animal or plant DNA binding protein.
- 15 11. A method according to Claim 9 wherein the DNA binding portion is all or a DNA-binding part of a bacterial or yeast DNA binding protein engineered to bind plant or animal genome.
- 20 12. A method according to any one of Claims 2 to 10 wherein the DNA binding portion is all or a DNA binding part of a steroid hormone receptor protein.
- 25 13. A method according to Claim 12 wherein the steroid hormone receptor protein is all or a DNA-binding portion of estrogen receptor (ER) or all or a DNA-binding portion of androgen receptor (AR).

14. A method according to Claim 3 wherein the RNA binding protein binds to nascent RNA expressed from proviral DNA.

15. A method according to Claim 14 wherein the RNA binding protein is *tat* or a *tat*-like protein or an RNA-binding portion thereof.

16. A method according to any one of Claims 1 to 15 wherein the nucleic acid binding portion and the chromatin inactivation portion are fused.

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17. A method according to any of the preceding claims wherein the eukaryotic cell is an animal cell and is contained within an animal or is a plant cell and is contained within a plant.

18. A method according to any of the preceding claims wherein the expression of a selected gene in a human is suppressed.

19. A method according to any of the preceding claims wherein the expression of a plurality of selected genes is suppressed.

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20. Use of a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with a selected gene which site is present in a eukaryotic genome and a chromatin inactivation portion in the manufacture of an agent for suppressing the expression of the selected gene in eukaryotic cell.

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21. Use of a polynucleotide encoding a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with a

selected gene which site is present in a plant or animal genome and a chromatin inactivation portion in the manufacture of an agent for suppressing the expression of the selected gene in a eukaryotic cell.

- 5 22. Use according to Claim 20 or 21 wherein the agent is a medicament for suppressing the expression of a selected gene in an animal.

23. A method of treating a patient in need of suppression of the expression of a selected gene, the method comprising administering to the
10 patient an effective amount of a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with the selected gene and a chromatin inactivation portion.

24. A method of treating a patient in need of suppression of the
15 expression of a selected gene, the method comprising administering to the patient an effective amount of a polynucleotide encoding a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with the selected gene and a chromatin inactivation portion.

20 25. Use of a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with a selected gene and a chromatin inactivation portion in the manufacture of a medicament for suppressing the expression of a selected gene in a patient in need of such suppression.

25 26. Use of a polynucleotide encoding a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with a selected gene and a chromatin inactivation portion in the manufacture of a

medicament for suppressing the expression of a selected gene in a patient in need of such suppression.

27. A polypeptide comprising a nucleic acid binding portion which
5 binds to a site at or associated with a selected gene and a chromatin inactivation portion for use in medicine.

28. A pharmaceutical composition comprising a polypeptide comprising
a nucleic acid binding portion which binds to a site at or associated with a
10 selected gene and a chromatin inactivation portion and a pharmaceutically acceptable carrier.

29. A polypeptide for use in medicine according to Claim 27 or a
pharmaceutical composition according to Claim 28 wherein the
15 polypeptide is as defined in any one of Claims 1 to 16.

30. A polynucleotide encoding a polypeptide comprising a nucleic acid
binding portion which binds to a site at or associated with a selected gene
and a chromatin inactivation portion for use in medicine.

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31. A pharmaceutical composition comprising a polynucleotide
encoding a polypeptide comprising a nucleic acid binding portion which
binds to a site at or associated with a selected gene and a chromatin
inactivation portion and a pharmaceutically acceptable carrier.

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32. A polypeptide comprising a nucleic acid binding portion which
binds to a site present in a eukaryotic genome and a chromatin inactivation
portion provided that when the nucleic acid binding portion is a DNA

binding portion of RAR α the chromatin inactivation portion is not a portion of PLZF protein and is not a portion of PML protein; and provided that when the nucleic acid binding portion is a DNA binding portion of the *Saccharomyces cerevisiae* GAL4 protein the chromatin inactivation portion is not a portion of PLZF protein, the C-terminal domain of vErbA, T₃R, T₃R β 1 or RAR, or N-CoR or a portion of N-CoR; and provided that when the nucleic acid binding portion is a DNA binding portion of the *Escherichia coli* LexA the chromatin inactivation portion is not mSin3, or the C-terminal domain of T₃R α or RAR α .

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33. A polypeptide according to Claim 32 wherein the nucleic acid binding portion or the chromatin inactivation portion are as defined in any one of Claims 1 to 16.

15 34. A polynucleotide encoding a polypeptide according to claim 32 or 33.

35. A method according to any one of claims 1 to 19 or polynucleotide according to claim 34 wherein the polynucleotide comprises a promoter operably linked to allow expression of the polypeptide.

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36. A method or polynucleotide according to Claim 35 wherein the promoter is an inducible promoter.

25 37. A vector comprising a polynucleotide according to any one of claims 34 to 36.

38. A method according to any of claims 1 to 19 or 35 to 36 wherein the polynucleotide is a vector comprising a polynucleotide as defined in any of claims 1 to 16 or 34 to 36.

5 39. A method according to Claim 38 or vector according to claim 37 wherein the vector is an animal cell vector.

40. A method according to claim 38 or vector according to claim 37 wherein the vector is a plant cell vector.

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41. A method according to any one of Claims 38 to 40 or vector according to claim 37, 39 or 40 wherein the vector is a viral vector.

42. A method according to any one of Claims 38 to 40 or vector
15 according to claim 37, 39 or 40 wherein the vector is a plasmid vector.

43. A polynucleotide for use in medicine according to Claim 30 or a pharmaceutical composition according to Claim 31 wherein the polynucleotide is a polynucleotide as defined in any one of claims 1 to 16
20 or 34 to 36 or a vector as defined in any one of claims 37 or 39 to 42.

44. A host cell comprising a polynucleotide according to any one of Claims 34 to 36 or a vector according to any one of Claims 37 or 39 to 42.

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45. A host cell according to Claim 44 which is a bacterial cell.

46. A host cell according to Claim 44 which is an animal cell.

47. A host cell according to Claim 44 which is a plant cell.
48. An animal comprising a host cell according to Claim 56.
- 5 49. A plant comprising a host cell according to Claim 47.
50. Any novel method of suppressing the activity of a selected gene in a plant or animal cell as herein described.
- 10 51. Any novel polypeptide which suppresses the activity of a selected gene in a plant or animal cell as herein described.
52. Any novel polynucleotide encoding a polypeptide which suppresses
15 the activity of a selected gene in a plant or animal cell as herein described.